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14. ABSTRACT
The goal of this project is to use recently developed 3D shape acquisition technologies and advanced computational techniques to define the autism face and determine whether there is a statistically significant facial phenotype. During this report period, we had generated a set of precise, highly replicable 3D anthropometric data for core ASD children and age-matched, typically developing controls, which has not previously been done. We had conducted preliminary facial pattern analysis and preliminary results suggest that there are subgroups of individuals with ASD that display distinct facial phenotypes.

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Introduction

This project will address whether the core group of idiopathic autism, often called essential autism is neurodevelopmental. We have observed clinically that children in the core population have a common facial gestault, which can be described as physically pleasing with wide spaced, deep set eyes and a broad forehead. The phenotype is subtle, not generally outside 2SD, so not easily catagorized by standard measurements. Study of this facial gestault is considered potentially informative since children with complex ASDs are often hyperteloric and facial dysmorphogeneis can serve as an index of brain dysmorphogenesis. This project will use recently developed 3D shape acquisition technologies and advanced computational techniques to define the autism face and determine whether there is a statistically significant facial phenotype.

Body

Overview

We had finished all the proposed tasks scheduled in this report period (07/01/2008 to 06/30/2009) in the revised statement of work (attached in the Appendices section). We had also conducted preliminary data analysis of task 4 scheduled between 07/01/2009 to 06/30/2010. In the following, we will describe each of the finished tasks in details.

TASK 1: 3DMD® cranial system procurement and installation

We had obtained internal funding from our university and had purchased the 3DMD® cranial system (Figure 1) for this project. It is currently installed in the Thompson Center for Autism in University of Missouri.

Figure 1: 3DMD® cranial system (http://www.3dmd.com/).

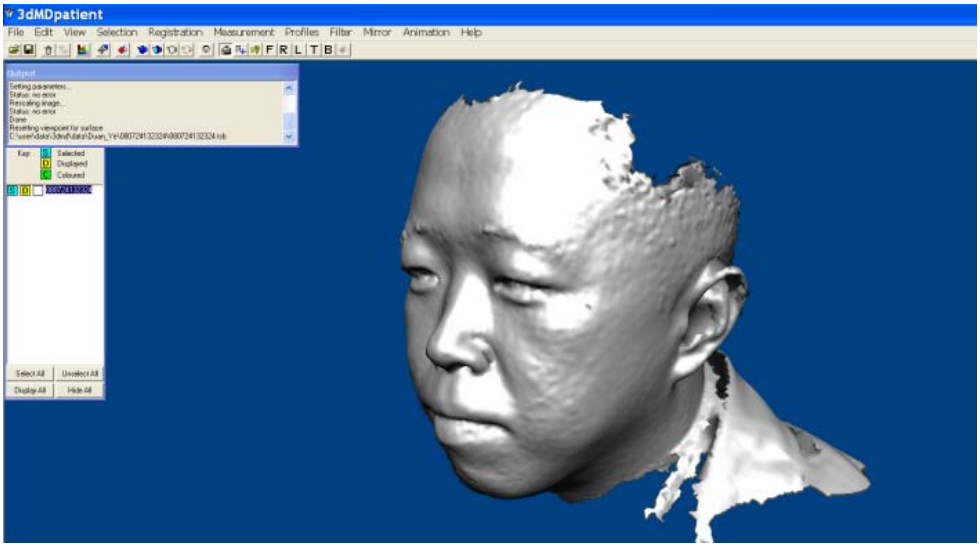
TASK 2: Subjects/Controls recruiting and selection

We had obtained IRB approval for our project, and had recruited 40 subjects and 72 age-matched, typically developing controls. The subjects are recruited from our large clinic population in the Thompson Center for Autism in University of Missouri. The age range is between 8 to 12 years old.

TASK 3: 3D surface data acquisition and facial feature extraction

We conducted full 360 degree head/face scan using the 3DMD® cranial system for all the subjects and controls recruited for the project. A 3D surface model with both the geo metry and the co-registered texture image is obtained for each subject (Figure 2).

(a)



(b)

Figure 2: An exam ple of the 3D sur face model of the PI wi th both the geom etry (b) and the co - registered texture image (a) obtained using the 3DMD® cranial system.

After the 3D face scan, we use the 3DMD patient® software to obtain 3D coordinate data for a suite of anthropometric facial landmarks (Figure 2), following [1]. Figure 3 shows an example of using the 3DMD patient® software to calculate the intercanthal distance between landmarks "en-en" of Figure 2.

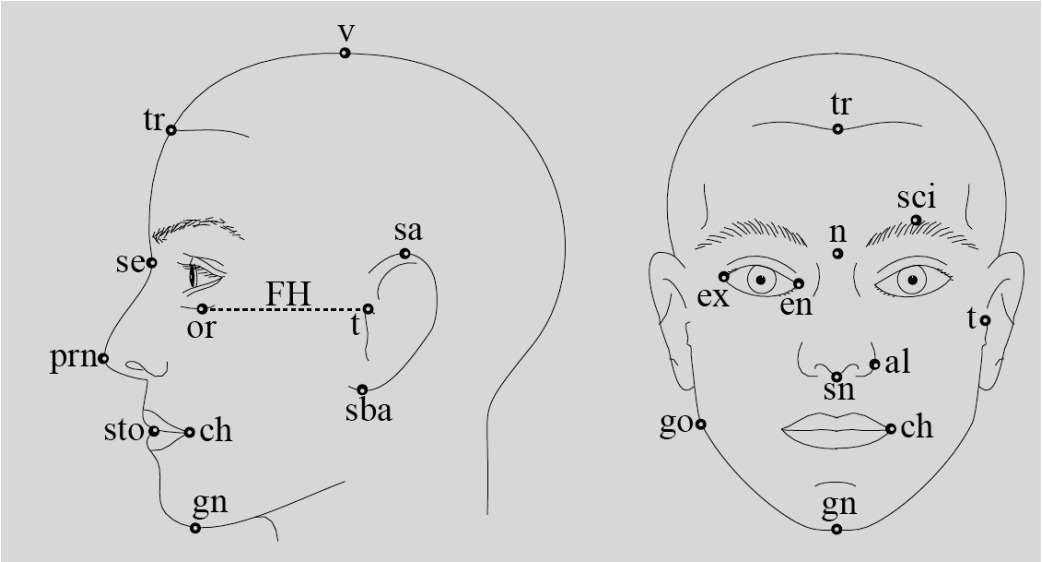


Figure 2: Anthropometric landmarks and measurements on face [1].

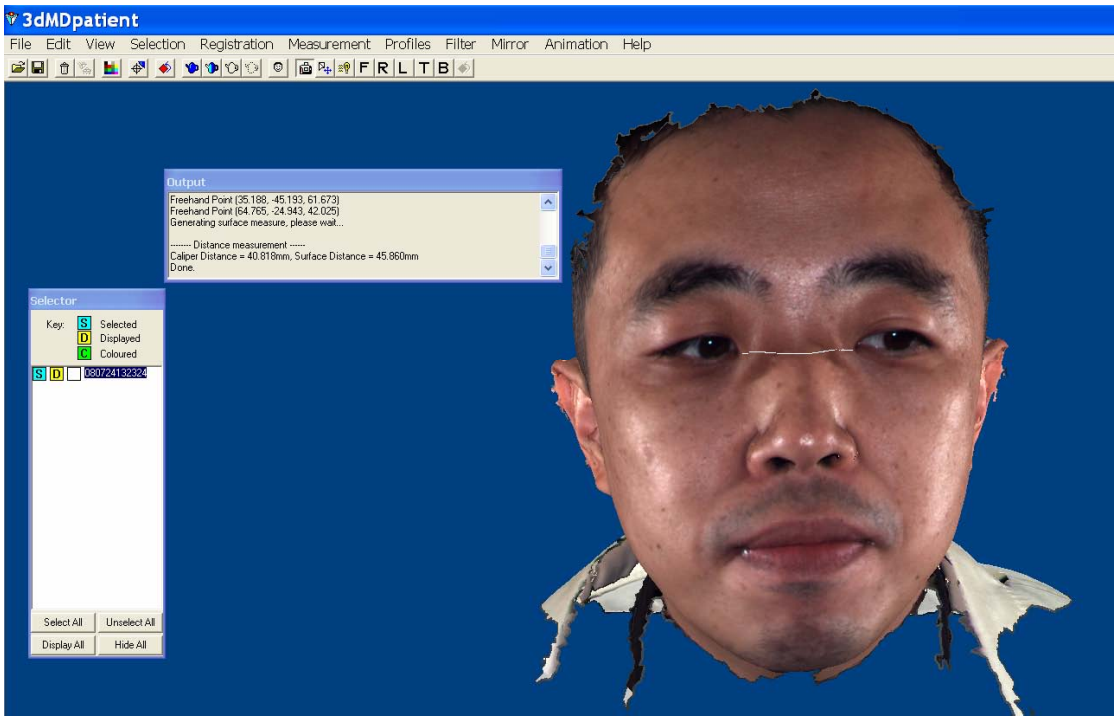


Figure 3: A n exam ple of m easuring the distan ces between anthropometric facial landm arks defined in [1] using the 3DMD patient® softwa re. Here the in tercanthal d istance between landmarks "en-en" (Figure 2) is measured.

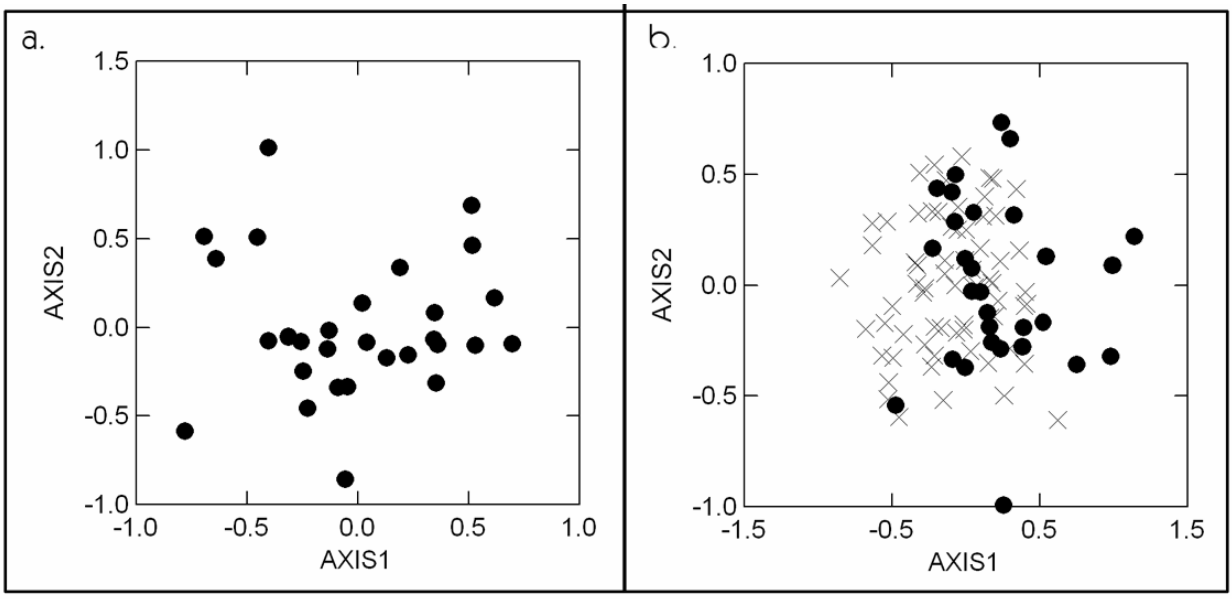
TASK 4: Facial phenotype exploration and correlation with clinical observations

We had conducted preliminary data analysis for facial phenotype exploration. We collected 19 anthropometric landmarks (Table 1) from the 3dMD images from all individuals with the observer blinded to clinical diagnosis. We used a form of principal coordinates analysis (PCOORD), which is a clustering method developed specifically for landmark data [2]. This analysis enables investigation of how salient features of facial anatomy combine on a multivariate axis to define similarities (and dissimilarities) among shapes. The goal is to identify the specific combination of morphological variables that successfully separate individuals into groups by projecting them onto the multivariate space. The computational details of principal coordinates analysis can be found in Krzanowski [3].

Phenotype	Anthropometric measurement
Broad forehead	ft-ft; ft-ft / tr-g
Wide nasal bridge	en-en / al-al
Hypertelorism	en-en; en-en / t-t; en-en / eu-eu
Almond-shaped eyes	en-ex / ps-pi
Wide philtrum	cph-cph; cph-cph / ch-ch
Pointed chin	go-gn / go-go; sn-gn / go-go
Outstanding helices	sa-sa /t-t

Table 1 - anthropometric landmarks facial features studied in this project.

We performed PCOORD analysis on the anthropometric data collected from the faces of the 29 individuals with ASD for whom we have completed data collection. In order to control for effects of size, each individual's data were scaled by the geometric mean of all possible linear distances between landmarks, following. The first two principal axes are illustrated in Figure 4. The first and second principal axes account for approximately 19.12% and 17.88% of the variation within the study sample, respectively. Note that several individuals on the high negative end of the first axis and high positive end of the second axis cluster separately from the main group overall (top left of Figure 4a). Suites of linear distances that are highly correlated with this location on these axes describe the shape of the mouth and the mouth's relative location within the face as a whole. These individuals display a wider philtrum and wider mouth overall relative to the rest of the face as compared to the remainder of the individuals in this sample. Also, the mouth is located in a more superior position relative to the upper and midface, such that is closer to the nose. As the data have been scaled for size, this is not an effect of age or growth.



(a) (b)

Figure 4: Preliminary facial feature clustering result for ASD based on principal coordinates analysis (PCOORD). (a) is the clustering result within the ASD group, (b) is the clustering result by combining the ASD group (shown as dot) and the control group (shown as X) together. Only the first two principal axes are shown here. See text for more descriptions.

Though this subgroup of individuals appears to be outside of the range of phenotypes of the majority of the individuals in our sample, we cannot know from this analysis whether the individuals in the subgroup or the main group are more representative of the typically-developing facial phenotype. To answer this question we must include the same data for both individuals with ASD and typically-developing individuals. Thus, we performed the same PCOORD analysis with the 29 individuals with ASD and included in the analysis data acquired from 69 typically-developing individuals. These data were also scaled to control for the effects of size. The first two principal axes are illustrated in Figure 4b. First, the majority of individuals with ASD cluster together with the typically-developing individuals. However, we see several individuals located on the high positive end of the first axis, with this axis accounting for approximately 18.65% of the variation in the sample. Again, these data were scaled prior to analysis, which indicates that the distribution of individuals is not based on age- or growth-related differences; in fact, the individuals included in this cluster are the same individuals that clustered separately in the analysis of only the individuals with ASD. Additionally, the suites of linear distances that define this subgroup closely match those from the previous analysis, i.e., the breadth of the philtrum and mouth, and the more superiorly-located mouth.

The results of these analyses suggest that there are subgroups of individuals with ASD that display distinct facial phenotypes. Study of additional individuals will show whether there are further subgroups based on these facial characteristics.

Key Research Accomplishments

- We had generated a set of pr ecise, highly replicable 3D anthropometric data for core ASD children and age-matched, typically deve loping controls, which has not previously been done.
- Preliminary results of facial pattern anal yses suggest that there are subgroups of individuals with ASD that display distinct facial phenotypes.

Reportable Outcomes

- We had collected 3D surface model with both the geometry and the co-registered texture image is obtained for 40 ASD subjects and 72 age-matched, typically developing controls. We will make the data available for the public.
- Preliminary results of facial pattern analyses suggest that there are subgroups of individuals with ASD that display distinct facial phenotypes.

Conclusion

We had generated a set of precise, highly rep licable 3D anthropom etric data for core ASD children and age-m atched, typically developing c ontrols, which has not previously been done. Preliminary results of facial patt ern analyses suggest that there are subgroups of individuals with ASD that display d istinct faci al phenotypes. Characterization of the facial phenotype will enhance understanding of em bryologic forces which can cause autism , and m ay provide a potential prescreening tool to assist early diagnosis.

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